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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Padigaru *et al.*

SERIAL NUMBER: 09/800,321 EXAMINER: M. Yu

FILING DATE: March 5, 2001 ART UNIT: 1642

FOR: NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

#22
4-16-03

Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

I, Valerie Gerlach hereby declare and state as follows:

1. I am employed by CuraGen, Inc., the assignee of this application. My title is senior research scientist. I received a Ph.D. in Cellular and Molecular Biology in 1996 from the University of Wisconsin-Madison. I was a post-doctoral fellow in the laboratory of Dr. Errol Friedberg at the University of Texas Southwestern Medical Center in Dallas, Texas from 1996 to 2000.

2. I have read, and am familiar with, the contents of the United States patent application entitled "Novel Proteins And Nucleic Acids Encoding Same", serial number 09/800,321, filed March 05, 2001. I understand that the pending claims are directed to an isolated polypeptide comprising SEQ ID NO:4.

3. I am aware that the Examiner has issued an Office Action. In particular, I understand that the Examiner has rejected the pending claims under 35 U.S.C. §§ 101 and 112, contending that the pending claims are not supported by either a credible, specific and substantial asserted utility or a well-established utility.

4. I make this declaration to rebut the Examiner's assertions under 35 U.S.C. §§ 101 and 112, with which I do not agree. It is my opinion that the claimed compositions have a credible, specific and substantial utility for at least the following reasons.

5. The specification states that the proteins of NOV1, including NOV1b (SEQ ID NO: 4) are useful as therapeutics in various NOV- or olfactory receptor (OR)-related pathologies and/or disorders. The NOV1 proteins are also useful in diagnostic or prognostic assays for various diseases and disorders, including cancers. *See e.g.*, specification at page 22, line 15 through page 23, line 7; specification at page 141, line 32 through page 142, line 15.

6. I have analyzed, or have had analyzed under my supervision, studies evaluating the quantitative expression of the nucleic acid sequence (Accession Number dj408b20B-1or "CG55343-01") encoding the claimed polypeptide of SEQ ID NO:4 in tissue culture cells and in isolated normal and pathological human tissue.

7. In a first study, expression of the CG55343-01 gene, encoding a protein with homology to olfactory receptors, was highest in breast cancer cell line MCF-7 (CT = 32-32.8). This gene was highly expressed in cancer cell lines than in normal tissues. Specifically, expression of CG55343-01 was significantly up-regulated in 3 out of 5 breast cancer cell lines, 2 out of 6 ovarian cancer cell lines, and 7 out of 10 lung cancer cell lines when compared to their appropriate normal controls. Results from three experiments using two distinct probe/primer sets were in good agreement. *See* Appendix, Table 3. Thus, expression of this gene or gene product has utility as a biological marker to detect breast, ovarian and lung cancers. In addition, inhibition of the activity or expression of the CG55343-01 gene and gene product using a monoclonal antibody or small molecule drug are useful in the treatment of breast, ovarian and lung cancer.

8. In a second study, expression of the CG55343-01 gene was significantly up-regulated in 6 out of 8 breast cancer samples in the panel. In addition, expression of this gene was higher in one ovarian and one bladder cancer sample when compared to their normal adjacent tissue. Results from four experiments using two distinct probe/primer sets were in good agreement. *See* Appendix, Table 4. These results are consistent with what was observed in the first study described above. Thus, expression of this gene or gene product has utility as a biological marker to detect breast, ovarian or bladder cancer. In addition, inhibition of the

activity or expression of the CG55343-01 gene and gene product using a monoclonal antibody or small molecule drug are useful in the treatment of breast, ovarian or bladder cancer.

9. In a third study, the CG55343-01 gene was expressed at low, but significant levels in a number of cancer cell lines, including a subset of lung, colon, cervical and pancreatic cell lines. No breast cancer cell lines and only a single ovarian cancer cell line were represented on this panel. Results were consistent with what was observed in the first study described above. *See* Appendix, Table 5.

10. The results of these studies, in my opinion, demonstrate that nucleic acid or the polypeptides encoded therefrom (SEQ ID NO:4) are useful in diagnostic and therapeutic applications in cancer (*e.g.*, breast, lung, ovarian and bladder). Thus, I believe that the Examiner should withdraw the rejection and allow the pending claims.

11. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements, and the like, so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18, United States Code, and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Valerie Gerlach
Valerie Gerlach

Signed at Branford CT
this 7th day of April 2003

APPENDIX

Materials and Methods: Quantitative expression analysis of CG55343-01 in various cells and tissues by RTQ-PCR

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR). RTQ PCR was performed on an Applied Biosystems ABI PRISM® 7700 or an ABI PRISM® 7900 HT Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing normal tissues and cancer cell lines), Panel 2 (containing samples derived from tissues from normal and cancer sources), Panel 3 (containing cancer cell lines), Panel 4 (containing cells and cell lines from normal tissues and cells related to inflammatory conditions), Panel 5D/5I (containing human tissues and cell lines with an emphasis on metabolic diseases), AI_comprehensive_panel (containing normal tissue and samples from autoinflammatory diseases), Panel CNSD.01 (containing samples from normal and diseased brains) and CNS_neurodegeneration_panel (containing samples from normal and Alzheimer's diseased brains).

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

First, the RNA samples were normalized to reference nucleic acids such as constitutively expressed genes (for example, β-actin and GAPDH). Normalized RNA (5 ul) was converted to cDNA and analyzed by RTQ-PCR using One Step RT-PCR Master Mix Reagents (Applied Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions.

In other cases, non-normalized RNA samples were converted to single strand cDNA (sscDNA) using Superscript II (Invitrogen Corporation; Catalog No. 18064-147) and random hexamers according to the manufacturer's instructions. Reactions containing up to 10 μg of total RNA were performed in a volume of 20 μl and incubated for 60 minutes at 42°C. This reaction can be scaled up to 50 μg of total RNA in a final volume of 100 μl. sscDNA samples are then normalized to reference nucleic acids as described previously, using 1X TaqMan® Universal Master mix (Applied Biosystems; catalog No. 4324020), following the manufacturer's instructions.

Probes and primers were designed for each assay according to Applied Biosystems Primer Express Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (Tm) range = 58°-60°C, primer optimal Tm = 59°C, maximum primer difference = 2°C, probe does not have 5'G, probe Tm must be 10°C greater than primer Tm, amplicon size 75bp to 100bp. The probes and primers selected (see below) were synthesized by Synthegen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900nM each, and probe, 200nM.

PCR conditions: When working with RNA samples, normalized RNA from each tissue and each cell line was spotted in each well of either a 96 well or a 384-well PCR plate (Applied Biosystems). PCR cocktails included either a single gene specific probe and primers set, or two multiplexed probe and primers sets (a set specific for the target clone and another gene-specific set multiplexed with the target probe). PCR reactions were set up using TaqMan® One-Step RT-PCR Master Mix (Applied Biosystems, Catalog No. 4313803) following manufacturer's instructions. Reverse transcription was performed at 48°C for 30 minutes followed by amplification/PCR cycles as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration

between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100.

When working with sscDNA samples, normalized sscDNA was used as described previously for RNA samples. PCR reactions containing one or two sets of probe and primers were set up as described previously, using 1X TaqMan® Universal Master mix (Applied Biosystems; catalog No. 4324020), following the manufacturer's instructions. PCR amplification was performed as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were analyzed and processed as described previously.

Panels 1, 1.1, 1.2, and 1.3D

The plates for Panels 1, 1.1, 1.2 and 1.3D include 2 control wells (genomic DNA control and chemistry control) and 94 wells containing cDNA from various samples. The samples in these panels are broken into 2 classes: samples derived from cultured cell lines and samples derived from primary normal tissues. The cell lines are derived from cancers of the following types: lung cancer, breast cancer, melanoma, colon cancer, prostate cancer, CNS cancer, squamous cell carcinoma, ovarian cancer, liver cancer, renal cancer, gastric cancer and pancreatic cancer. Cell lines used in these panels are widely available through the American Type Culture Collection (ATCC), a repository for cultured cell lines, and were cultured using the conditions recommended by the ATCC. The normal tissues found on these panels are comprised of samples derived from all major organ systems from single adult individuals or fetuses. These samples are derived from the following organs: adult skeletal muscle, fetal skeletal muscle, adult heart, fetal heart, adult kidney, fetal kidney, adult liver, fetal liver, adult lung, fetal lung, various regions of the brain, the spleen, bone marrow, lymph node, pancreas, salivary gland, pituitary gland, adrenal gland, spinal cord, thymus, stomach, small intestine, colon, bladder, trachea, breast, ovary, uterus, placenta, prostate, testis and adipose.

In the results for Panels 1, 1.1, 1.2 and 1.3D, the following abbreviations are used:

ca. = carcinoma,
* = established from metastasis,

met = metastasis,
s cell var = small cell variant,
non-s = non-sm = non-small,
squam = squamous,
pl. eff = pl effusion = pleural effusion,
glio = glioma,
astro = astrocytoma, and
neuro = neuroblastoma.

Panels 2D, 2.2, 2.3 and 2.4

The plates for Panels 2D, 2.2, 2.3 and 2.4 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI) or from Ardais or Clinomics). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologist at NDRI/ CHTN/Ardais/Clinomics). Unmatched RNA samples from tissues without malignancy (normal tissues) were also obtained from Ardais or Clinomics. This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissues were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

Panel 3D, 3.1 and 3.2

The plates of Panel 3D, 3.1, and 3.2 are comprised of 94 cDNA samples and two control samples. Specifically, 92 of these samples are derived from cultured human cancer cell lines, 2

samples of human primary cerebellar tissue and 2 controls. The human cell lines are generally obtained from ATCC (American Type Culture Collection), NCI or the German tumor cell bank and fall into the following tissue groups: Squamous cell carcinoma of the tongue, breast cancer, prostate cancer, melanoma, epidermoid carcinoma, sarcomas, bladder carcinomas, pancreatic cancers, kidney cancers, leukemias/lymphomas, ovarian/uterine/cervical, gastric, colon, lung and CNS cancer cell lines. In addition, there are two independent samples of cerebellum. These cells are all cultured under standard recommended conditions and RNA extracted using the standard procedures. The cell lines in panel 3D, 3.1, 3.2, 1, 1.1., 1.2, 1.3D, 1.4, 1.5, and 1.6 are of the most common cell lines used in the scientific literature.

Results: CG55343-01 Olfactory Receptor (Novlb)

Expression of gene CG55343-01 was assessed using the primer-probe sets Ag1592 and Ag457, described in Tables 1 and 2. Results of the RTQ-PCR runs are shown in Tables 3, 4 and 5.

Table 1. Probe Name Ag1592

Primers	Sequences	Length	Start Position
Forward	5'-aggaccaaggaaagatggttt-3'	21	804
Probe	TET-5'-tgcacccatgctgaatccccttatat-3'-TAMRA	26	844
Reverse	5'-aagccttcctttacctccttgt-3'	22	882

Table 2. Probe Name Ag457

Primers	Sequences	Length	Start Position
Forward	5'-gccgtctctgtgtacctgca-3'	20	764
Probe	TET-5'-ttcgcccagctccaaggaccaa-3'-TAMRA	22	790
Reverse	5'-ttccatagaagagagaaaccatctttc-3'	27	813

Table 3. Panel 1.3D

Column A - Rel. Exp.(%) Ag1592, Run 152066536 Column B - Rel. Exp.(%) Ag457, Run 146581824 Column C - Rel. Exp.(%) Ag457, Run 151104452							
Tissue Name	**A**	**B**	**C**	**Tissue Name**	**A**	**B**	**C**
Liver adenocarcinoma	0.0	0.8	0.0	Kidney (fetal)	1.3	0.0	2.1
Pancreas	0.0	0.0	4.0	Renal ca. 786-0	0.0	0.0	0.0
Pancreatic ca. CAPAN 2	0.0	1.3	2.1	Renal ca. A498	8.5	9.5	10.6
Adrenal gland	3.5	1.4	0.0	Renal ca. RXF 393	0.0	0.0	0.0
Thyroid	0.0	0.0	0.9	Renal ca. ACHN	0.0	0.6	0.0
Salivary gland	0.0	0.0	2.3	Renal ca. UO-31	0.0	0.0	0.0
Pituitary gland	0.0	0.0	0.0	Renal ca. TK-10	1.7	1.6	0.9
Brain (fetal)	0.0	0.0	0.0	Liver	2.5	2.0	1.8
Brain (whole)	0.0	1.5	0.0	Liver (fetal)	6.3	5.7	12.7
Brain (amygdala)	1.4	1.5	0.0	Liver ca. (hepatoblast) HepG2	9.5	5.3	6.1
Brain (cerebellum)	1.8	0.0	2.0	Lung	1.5	0.7	1.9
Brain (hippocampus)	1.2	0.0	0.0	Lung (fetal)	2.3	4.0	5.6
Brain (substantia nigra)	1.2	0.0	2.5	Lung ca. (small cell) LX-1	3.4	2.9	4.0
Brain (thalamus)	0.0	0.0	0.0	Lung ca. (small cell) NCI-H69	10.8	15.6	14.4
Cerebral Cortex	0.0	1.5	2.1	Lung ca. (s.cell var.) SHP-77	21.2	33.9	21.3
Spinal cord	0.0	0.0	0.0	Lung ca. (large cell)NCI-H460	5.2	2.0	2.6
glio/astro U87-MG	4.5	1.5	1.4	Lung ca. (non-sm. cell) A549	0.0	3.6	4.5
glio/astro U-118-MG	18.9	11.4	20.2	Lung ca. (non-s.cell) NCI-H23	18.3	7.6	14.6
astrocytoma SW1783	5.3	2.0	3.0	Lung ca. (non-s.cell) HOP-62	0.0	0.0	0.0
neuro*; met SK-N-AS	7.1	4.5	14.1	Lung ca. (non-s.cl) NCI-H522	18.0	7.0	17.3
astrocytoma SF-539	2.6	0.7	2.9	Lung ca. (squam.) SW 900	0.0	1.5	1.5
astrocytoma SNB-75	9.5	22.7	17.4	Lung ca. (squam.) NCI-H596	14.0	17.4	26.2
glioma SNB-19	0.0	1.8	0.0	Mammary gland	1.6	0.0	0.0
glioma U251	0.0	1.3	0.0	Breast ca.* (pl.ef) MCF-7	**100.0**	**100.0**	**100.0**
glioma SF-295	4.6	1.2	4.5	Breast ca.* (pl.ef) MDA-MB-231	21.0	24.5	19.8
Heart (fetal)	5.6	0.4	3.1	Breast ca.* (pl.ef) T47D	5.9	2.1	1.7
Heart	0.0	0.0	1.2	Breast ca. BT-549	13.8	22.8	16.0
Skeletal muscle (fetal)	4.1	5.0	6.2	Breast ca. MDA-N	3.5	3.3	7.7
Skeletal muscle	0.0	0.0	0.9	Ovary	4.1	0.0	1.0
Bone marrow	8.5	3.7	2.2	Ovarian ca. OVCAR-3	8.7	10.5	5.3
Thymus	3.1	5.3	0.8	Ovarian ca. OVCAR-4	0.0	0.0	0.0

Spleen	1.6	0.7	1.1	Ovarian ca. OVCAR-5	11.7	6.3	4.9
Lymph node	1.1	1.4	2.3	Ovarian ca. OVCAR-8	1.5	2.2	2.9
Colorectal	4.0	0.4	5.5	Ovarian ca. IGROV-1	1.8	0.0	0.9
Stomach	1.4	1.4	6.5	Ovarian ca.* (ascites) SK-OV-3	1.2	1.3	0.8
Small intestine	0.0	0.0	1.7	Uterus	0.0	1.4	3.3
Colon ca. SW480	27.0	34.2	34.6	Placenta	11.1	9.5	11.4
Colon ca.* SW620(SW480 met)	2.5	6.1	11.8	Prostate	0.0	0.0	0.9
Colon ca. HT29	4.1	1.6	2.1	Prostate ca.* (bone met)PC-3	6.5	5.8	7.2
Colon ca. HCT-116	2.8	0.7	0.0	Testis	1.2	2.1	1.3
Colon ca. CaCo-2	4.6	6.2	6.3	Melanoma Hs688(A).T	0.0	0.0	1.3
Colon ca. tissue(ODO3866)	2.4	0.8	0.0	Melanoma* (met) Hs688(B).T	1.8	0.0	2.2
Colon ca. HCC-2998	4.9	5.9	1.6	Melanoma UACC-62	0.0	0.0	0.0
Gastric ca.* (liver met) NCI-N87	42.0	86.5	65.1	Melanoma M14	1.6	0.0	2.0
Bladder	3.2	1.4	3.2	Melanoma LOX IMVI	0.0	2.6	2.6
Trachea	0.0	0.0	0.0	Melanoma* (met) SK-MEL-5	0.0	0.0	0.0
Kidney	1.5	0.0	0.0	Adipose	0.0	0.0	0.0

Table 4. Panel 2D

Column A - Rel. Exp.(%) Ag1592, Run 152066737 Column B - Rel. Exp.(%) Ag457, Run 146087098 Column C - Rel. Exp.(%) Ag457, Run 146581925 Column D - Rel. Exp.(%) Ag457, Run 158141680				
Tissue Name	**A**	**B**	**C**	**D**
Normal Colon	0.0	1.6	0.8	3.6
CC Well to Mod Diff (ODO3866)	1.3	0.5	0.6	0.0
CC Margin (ODO3866)	0.0	2.4	2.0	2.5
CC Gr.2 rectosigmoid (ODO3868)	1.3	4.3	2.3	0.8
CC Margin (ODO3868)	0.9	0.0	0.7	1.1
CC Mod Diff (ODO3920)	4.3	6.3	6.7	4.0
CC Margin (ODO3920)	0.9	2.7	0.5	1.0
CC Gr.2 ascend colon (ODO3921)	2.7	1.6	1.7	0.0
CC Margin (ODO3921)	2.1	0.4	1.5	1.3
CC from Partial Hepatectomy (ODO4309) Mets	3.5	1.8	1.5	0.6
Liver Margin (ODO4309)	2.0	0.8	0.8	2.1

Colon mets to lung (OD04451-01)	4.1	0.0	0.4	0.6
Lung Margin (OD04451-02)	0.0	0.0	0.7	0.0
Normal Prostate 6546-1	2.2	3.4	3.1	1.4
Prostate Cancer (OD04410)	14.5	12.4	16.2	7.3
Prostate Margin (OD04410)	9.0	4.7	6.4	5.9
Prostate Cancer (OD04720-01)	0.0	0.1	0.4	1.1
Prostate Margin (OD04720-02)	0.0	1.0	0.9	2.9
Normal Lung 061010	2.2	1.2	2.5	1.7
Lung Met to Muscle (ODO4286)	3.5	4.2	3.4	4.2
Muscle Margin (ODO4286)	0.9	0.0	0.5	0.0
Lung Malignant Cancer (OD03126)	0.0	1.5	1.4	1.7
Lung Margin (OD03126)	0.0	0.9	2.6	1.5
Lung Cancer (OD04404)	6.0	4.1	3.5	6.8
Lung Margin (OD04404)	0.0	1.3	0.0	0.9
Lung Cancer (OD04565)	1.1	0.6	0.9	0.0
Lung Margin (OD04565)	0.0	1.2	0.4	0.7
Lung Cancer (OD04237-01)	17.9	15.9	14.0	15.7
Lung Margin (OD04237-02)	0.9	0.0	1.4	0.8
Ocular Mel Met to Liver (ODO4310)	0.0	0.3	0.0	0.0
Liver Margin (ODO4310)	0.0	0.7	1.6	2.9
Melanoma Mets to Lung (OD04321)	9.7	10.1	9.7	8.2
Lung Margin (OD04321)	0.0	2.3	1.0	0.0
Normal Kidney	1.6	0.6	0.7	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.8	0.0	0.4	0.7
Kidney Margin (OD04338)	1.4	0.0	0.0	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	0.6	0.0	1.4
Kidney Margin (OD04339)	0.0	0.0	0.7	0.0
Kidney Ca, Clear cell type (OD04340)	3.0	1.8	3.0	0.9
Kidney Margin (OD04340)	0.0	0.9	0.4	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	3.1	2.2	1.3
Kidney Margin (OD04348)	0.0	2.4	0.0	0.0
Kidney Cancer (OD04622-01)	0.0	0.9	0.8	1.6
Kidney Margin (OD04622-03)	0.0	0.8	0.0	0.0
Kidney Cancer (OD04450-01)	0.0	0.7	0.0	2.7
Kidney Margin (OD04450-03)	0.9	0.9	0.8	0.6
Kidney Cancer 8120607	0.0	0.0	0.4	0.0
Kidney Margin 8120608	0.0	0.5	0.3	0.8

Kidney Cancer 8120613	1.1	0.0	0.0	0.6
Kidney Margin 8120614	0.0	0.0	0.0	0.0
Kidney Cancer 9010320	0.0	0.4	1.3	0.0
Kidney Margin 9010321	0.0	0.8	0.0	0.0
Normal Uterus	0.0	0.0	0.0	0.0
Uterus Cancer 064011	0.8	1.2	2.8	1.6
Normal Thyroid	0.0	0.4	2.6	0.0
Thyroid Cancer 064010	1.1	0.0	1.5	0.0
Thyroid Cancer A302152	2.0	3.2	2.2	1.9
Thyroid Margin A302153	0.8	0.0	0.7	0.0
Normal Breast	0.0	0.2	0.4	1.5
Breast Cancer (OD04566)	4.6	8.4	9.9	15.3
Breast Cancer (OD04590-01)	87.1	**100.0**	87.7	59.9
Breast Cancer Mets (OD04590-03)	36.3	38.7	55.9	14.8
Breast Cancer Metastasis (OD04655-05)	17.3	17.6	22.4	8.1
Breast Cancer 064006	6.3	5.4	3.4	4.3
Breast Cancer 1024	17.3	20.6	20.9	18.7
Breast Cancer 9100266	3.8	5.4	2.7	3.7
Breast Margin 9100265	3.0	0.8	0.4	2.5
Breast Cancer A209073	2.2	2.7	1.3	0.0
Breast Margin A209073	0.7	0.0	1.7	0.9
Normal Liver	1.8	0.5	0.9	0.0
Liver Cancer 064003	2.0	0.4	0.8	0.0
Liver Cancer 1025	1.1	0.7	0.6	0.0
Liver Cancer 1026	0.0	0.9	0.0	0.0
Liver Cancer 6004-T	1.3	0.0	0.0	0.9
Liver Tissue 6004-N	3.6	0.8	1.4	1.1
Liver Cancer 6005-T	0.0	0.6	2.4	0.0
Liver Tissue 6005-N	2.3	0.4	1.2	1.8
Normal Bladder	7.9	7.1	3.4	2.0
Bladder Cancer 1023	0.0	0.0	0.0	1.0
Bladder Cancer A302173	4.2	4.2	1.8	11.9
Bladder Cancer (OD04718-01)	97.3	62.0	**100.0**	**100.0**
Bladder Normal Adjacent (OD04718-03)	0.0	0.9	0.4	0.0
Normal Ovary	1.1	0.0	0.0	0.8
Ovarian Cancer 064008	3.4	1.8	1.1	3.7
Ovarian Cancer (OD04768-07)	**100.0**	76.3	89.5	85.3

Ovary Margin (OD04768-08)	1.4	0.0	0.0	0.0
Normal Stomach	1.1	0.6	1.4	0.0
Gastric Cancer 9060358	0.0	0.3	0.0	0.9
Stomach Margin 9060359	2.4	0.5	0.8	0.0
Gastric Cancer 9060395	1.9	2.4	1.8	2.1
Stomach Margin 9060394	2.1	1.9	0.0	1.7
Gastric Cancer 9060397	10.9	11.7	10.0	8.7
Stomach Margin 9060396	0.0	1.0	0.5	1.2
Gastric Cancer 064005	4.9	0.6	5.6	2.8

Table 5. Panel 3D

Column A - Rel. Exp.(%) Ag457, Run 172134279			
Tissue Name	**A**	**Tissue Name**	**A**
Daoy- Medulloblastoma	8.5	Ca Ski- Cervical epidermoid carcinoma (metastasis)	24.0
TE671- Medulloblastoma	1.5	ES-2- Ovarian clear cell carcinoma	0.0
D283 Med- Medulloblastoma	1.0	Ramos- Stimulated with PMA/ionomycin 6h	0.0
PFSK-1- Primitive Neuroectodermal	0.8	Ramos- Stimulated with PMA/ionomycin 14h	1.2
XF-498- CNS	2.1	MEG-01- Chronic myelogenous leukemia (megokaryoblast)	24.1
SNB-78- Glioma	2.5	Raji- Burkitt's lymphoma	0.0
SF-268- Glioblastoma	1.3	Daudi- Burkitt's lymphoma	0.0
T98G- Glioblastoma	3.4	U266- B-cell plasmacytoma	25.9
SK-N-SH- Neuroblastoma (metastasis)	1.2	CA46- Burkitt's lymphoma	0.0
SF-295- Glioblastoma	1.2	RL- non-Hodgkin's B-cell lymphoma	0.0
Cerebellum	2.1	JM1- pre-B-cell lymphoma	1.3
Cerebellum	0.9	Jurkat- T cell leukemia	0.0
NCI-H292- Mucoepidermoid lung carcinoma	4.0	TF-1- Erythroleukemia	4.8
DMS-114- Small cell lung cancer	2.7	HUT 78- T-cell lymphoma	0.0
DMS-79- Small cell lung cancer	**100.0**	U937- Histiocytic lymphoma	19.9
NCI-H146- Small cell lung cancer	11.7	KU-812- Myelogenous leukemia	4.7
NCI-H526- Small cell lung cancer	5.3	769-P- Clear cell renal carcinoma	0.0
NCI-N417- Small cell lung cancer	7.0	Caki-2- Clear cell renal carcinoma	0.0
NCI-H82- Small cell lung cancer	0.0	SW 839- Clear cell renal carcinoma	0.0
NCI-H157- Squamous cell lung cancer	23.5	Rhabdoid kidney tumor	4.2

(metastasis)			
NCI-H1155- Large cell lung cancer	3.4	Hs766T- Pancreatic carcinoma (LN metastasis)	19.3
NCI-H1299- Large cell lung cancer	11.4	CAPAN-1- Pancreatic adenocarcinoma (liver metastasis)	10.2
NCI-H727- Lung carcinoid	0.0	SU86.86- Pancreatic carcinoma (liver metastasis)	1.2
NCI-UMC-11- Lung carcinoid	2.8	BxPC-3- Pancreatic adenocarcinoma	7.6
LX-1- Small cell lung cancer	3.4	HPAC- Pancreatic adenocarcinoma	2.8
Colo-205- Colon cancer	3.5	MIA PaCa-2- Pancreatic carcinoma	1.2
KM12- Colon cancer	11.4	CFPAC-1- Pancreatic ductal adenocarcinoma	25.7
KM20L2- Colon cancer	0.0	PANC-1- Pancreatic epithelioid ductal carcinoma	1.3
NCI-H716- Colon cancer	53.6	T24- Bladder carcinma (transitional cell)	3.3
SW-48- Colon adenocarcinoma	1.7	5637- Bladder carcinoma	0.0
SW1116- Colon adenocarcinoma	6.2	HT-1197- Bladder carcinoma	6.3
LS 174T- Colon adenocarcinoma	0.0	UM-UC-3- Bladder carcinma (transitional cell)	0.0
SW-948- Colon adenocarcinoma	0.0	A204- Rhabdomyosarcoma	5.0
SW-480- Colon adenocarcinoma	0.0	HT-1080- Fibrosarcoma	0.0
NCI-SNU-5- Gastric carcinoma	13.9	MG-63- Osteosarcoma	0.0
KATO III- Gastric carcinoma	6.8	SK-LMS-1- Leiomyosarcoma (vulva)	7.4
NCI-SNU-16- Gastric carcinoma	6.3	SJRH30- Rhabdomyosarcoma (met to bone marrow)	0.0
NCI-SNU-1- Gastric carcinoma	5.8	A431- Epidermoid carcinoma	4.8
RF-1- Gastric adenocarcinoma	2.6	WM266-4- Melanoma	0.0
RF-48- Gastric adenocarcinoma	0.0	DU 145- Prostate carcinoma (brain metastasis)	0.0
MKN-45- Gastric carcinoma	2.9	MDA-MB-468- Breast adenocarcinoma	7.1
NCI-N87- Gastric carcinoma	2.9	SCC-4- Squamous cell carcinoma of tongue	0.0
OVCAR-5- Ovarian carcinoma	5.3	SCC-9- Squamous cell carcinoma of tongue	0.8
RL95-2- Uterine carcinoma	5.9	SCC-15- Squamous cell carcinoma of tongue	0.0
HelaS3- Cervical adenocarcinoma	11.8	CAL 27- Squamous cell carcinoma of tongue	2.9

Panel 1.3D Summary: Ag457/Ag1592 Results from three experiments using two distinct probe/primer sets were in good agreement. Expression of the CG55343-01 gene, encoding a protein with homology to olfactory receptors, was highest in breast cancer cell line

MCF-7 (CT = 32-32.8). This gene is more highly expressed in cancer cell lines than in normal tissues. Specifically, expression of CG55343-01 is significantly upregulated in 3/5 breast cancer cell lines, 2/6 ovarian cancer cell lines, and 7/10 lung cancer cell lines when compared to the appropriate normal controls. Thus, expression of this gene can be used as a marker to distinguish breast, ovarian and lung cancers from normal tissue. In addition, inhibition of the activity of the CG55343-01 gene product using a monoclonal antibody or small molecule drug can be used in the treatment of breast, ovarian and lung cancer.

Panel 2D Summary: Ag457/Ag1592 Results from four experiments using two distinct probe/primer sets were in good agreement. Expression of the CG55343-01 gene was strikingly upregulated in 6/8 breast cancer samples. In addition, expression of this gene is higher in one ovarian and one bladder cancer sample when compared to the normal adjacent tissue. These results are consistent with what was observed on Panel 1.3D. Thus, expression of this gene can be used as a marker to distinguish breast, ovarian and bladder cancer from normal tissue. In addition, inhibition of the activity of the CG55343-01 gene product using a monoclonal antibody or small molecule drug can be used in the treatment of breast, ovarian and bladder cancer.

Panel 3D Summary: Ag457 Consistent with what was observed in Panel 1.3D, the CG55343-01 gene is expressed at low but significant levels in a number of cancer cell lines, including a subset of lung, colon, cervical and pancreatic cell lines. No breast cancer cell lines and only a single ovarian cancer cell line were represented on this panel.